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Probability Estimates for the Unique Childhood Leukemia Cluster in Fallon, Nevada, and Risks Near Other U.S. Military Aviation Facilities

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A unique cluster of childhood leukemia has recently occurred around the city of Fallon in Churchill County, Nevada. From 1999 to 2001, 11 cases were diagnosed in this county of 23,982 people. Exposures related to a nearby naval air station such as jet fuel or an infectious agent carried by naval aviators have been hypothesized as potential causes. The possibility that the cluster could be attributed to chance was also considered. We used data from the Surveillance, Epidemiology, and End Results Program (SEER) to examine the likelihood that chance could explain this cluster. We also used SEER and California Cancer Registry data to evaluate rates of childhood leukemia in other U.S. counties with military aviation facilities. The age-standardized rate ratio (RR) in Churchill County was 12.0 [95% confidence interval (CI), 6.0–21.4; *p* = 4.3 × 10^{-9}]. A cluster of this magnitude would be expected to occur in the United States by chance about once every 22,000 years. The age-standardized RR for the five cases diagnosed after the cluster was first reported was 11.2 (95% CI, 3.6–26.3). In contrast, the incidence rate was not increased in all other U.S. counties with military aviation bases (RR = 1.04; 95% CI, 0.97–1.12) or in the subset of rural counties with military aviation bases (RR = 0.72; 95% CI, 0.48–1.08). These findings suggest that the Churchill County cluster was unlikely due to chance, but no general increase in childhood leukemia was found in other U.S. counties with military aviation bases. ***Key words:*** **ALL, childhood cancer, cluster, leukemia, military.** ***Environ Health Perspect*** **112:766–771 (2004). doi:10.1289/ehp.6592 available via** ***http://dx.doi.org/*** **[Online 2 February 2004]**

Leukemia is the most common cancer diagnosed in children < 19 years of age (Ries et al. 2003). Several factors have been associated with increased rates of childhood leukemia, including ionizing radiation, Down syndrome, and certain inherited and congenital conditions (Little 1999). However, known causes explain only a small fraction of all cases of leukemia.

This article was prompted by a recent cluster of leukemia cases occurring near the naval air station in Fallon (NAS Fallon), Churchill County, a sparsely populated area in western Nevada. From 1999 to 2001, 11 cases of childhood leukemia were diagnosed among children residing in Churchill County at the time of diagnosis. An additional five cases have been identified from 1997 to 2002 among children who were not residents at the time of diagnosis but who lived in Churchill County at some point before diagnosis [Nevada State Health Division (NSHD) 2003]. In the preceding 20 years, only one case of childhood leukemia was reported to the Nevada Central Cancer Registry among Churchill County residents (Moore et al. 2002). This dramatic increase in the number of cases, the short time frame in which the cases were diagnosed, and the small population of the source area all highlight the unusual nature of this cancer cluster.

Initially hypothesized causes of the Churchill County cluster included chemical exposures such as jet fuel or benzene, drinking water contamination by a radioactive isotope or naturally occurring arsenic, population mixing, or a new infectious agent, potentially associated with the nearby naval air station (NSHD 2003). Jet fuel has been associated with immune system effects in several studies (Harris et al. 1997a, 1997b, 2000, 2001; Jackman et al. 2002; Rhodes et al. 2003; Ullrich 1999), and benzene, a minor component of jet fuel, has been associated with increased rates of leukemia in occupationally exposed cohorts (Hayes et al. 2001; Savitz and Andrews 1997). The population-mixing theory holds that childhood leukemia can occur as a rare end result of some yet unknown infectious process, and large-scale mixing of urban and rural groups leads to increases in leukemia by allowing increased contact between potentially susceptible and infected individuals (Kinlen 1995). In fact, large-scale movements of people into rural areas have been associated with increased rates of childhood leukemia in many studies (Dickinson and Parker 1999; Kinlen 1988; Kinlen and Hudson 1991; Kinlen and John 1994; Kinlen et al. 1990, 1993).

Churchill County is highly rural, with a population of 23,982 people in an area of 5,023 square miles (U.S. Census Bureau 2003a). NAS Fallon lies within this county and conducts several large military training operations. Annually, approximately 55,000 military personnel visit NAS Fallon for training, each staying an average of 14 days (U.S. Navy 2002a). This large and rapid movement of military aviators and other personnel in and out of Churchill County, many arriving from a wide range of international locations, provides opportunity for the introduction of a diverse array of new infective agents.

The Centers for Disease Control and Prevention (CDC) has recently completed the first portion of a large cross-sectional investigation of the Churchill County cluster (CDC 2003). More than 100 biologic measurements and more than 200 environmental measurements have been collected and analyzed. Despite this extensive testing, no obvious cause of the cluster has been identified. Further information on the CDC investigation and the cluster is available online through the Nevada State Health Division (NSHD 2003).

The goal of the present analysis was 2-fold. The first was to evaluate the possibility that the Churchill County cluster could be attributed to random chance. The second was to evaluate whether other areas with military aviation bases have experienced increased rates of childhood leukemia similar to those occurring in Churchill County. As discussed by several authors, routine tests of statistical significance may not be appropriate in the *post hoc* analysis of clusters, because the specific location and time frame being assessed are defined by the cluster and are not set *a priori* (Neutra 1990; Neutra et al. 1992; Rothman 1990; Waller 2000). However, an important feature of the Churchill County cluster was that many of the cases were diagnosed after the State of Nevada began its investigation in July 2000 (Todd 2001). Thus, the investigation of this cluster was not entirely *post hoc*. Because of this, an *a priori* hypothesis regarding increased leukemia rates can be tested by confining the

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analyses to the time period after the state investigation had begun.

Materials and Methods

Age-standardized incidence rate ratios (RRs) for childhood leukemia in Churchill County were calculated separately for the cluster as a whole and for the time period that only included cases diagnosed after investigation of the cluster had begun in July 2000. In both analyses, cases were defined as children 0–19 years of age with leukemia confirmed by bone marrow biopsy who lived in Churchill County at the time of diagnosis. For the cluster as a whole, an age-standardized incidence RR was estimated for the years 1999–2001. For the five cases diagnosed after the investigation had begun, an age-standardized incidence RR was calculated for the period beginning July 2000 and ending December 2001. In both analyses, RRs were estimated by comparing the observed number of cases with the expected number based on the most recent age-specific rates from the Surveillance, Epidemiology, and End Results Program (SEER). Population data in 5-year age groups for Churchill County were obtained from the 2000 U.S. Census (U.S. Census Bureau 2003a). Confidence intervals were calculated using the methods described by Breslow and Day (1987), and *p*-values were calculated using the Poisson probability distribution model (Checkoway et al. 1989).

Rates of childhood leukemia in counties with military aviation bases (base counties) were compared with rates in counties without military bases (nonbase counties) using all counties covered by SEER and the California Cancer Registry (CCR). These registries were chosen because they are the largest cancer registries in the United States and both provide readily accessible yearly cancer incidence data on a county level [California Cancer Registry 2000; National Cancer Institute (NCI) 2001]. SEER provides cancer incidence data for five states and four metropolitan areas, representing approximately 9% of the U.S. population, for 1973–1999. The CCR provides cancer incidence data for approximately 97% of the population in California for 1992–1998.

The goal in selecting base counties was to choose areas with military facilities similar to NAS Fallon. All active naval air stations and Air Force bases in U.S. counties covered by SEER and CCR were identified using publicly available data provided by the U.S. Navy and Air Force (U.S. Air Force 2003; U.S. Navy 2003). Counties with facilities where the type of aircraft, or volume of air traffic, were substantially different than NAS Fallon were excluded from the analysis. These included Air National Guard bases, Air Force Reserve bases, Marine Corp air stations, outlying fields, Army air fields, and Navy air landing facilities. Air Force bases where the primary mission was space or missile technology were also excluded. All other Air Force bases and naval air stations in the selected counties were included in the analysis.

Rates of childhood leukemia in base counties were compared with those in nonbase counties. Analyses were performed for all types of childhood leukemia combined and separately for acute lymphocytic leukemia (ALL). In the first analysis, incidence RR estimates were calculated for four individual age groups (0–4, 5–9, 10–14, and 15–19 years). Leukemia rates were estimated for all base counties combined by dividing the sum of all the cases diagnosed in the base counties by the sum of the age-specific populations of these counties. Yearly population estimates provided by SEER and CCR were used for these calculations. Similar calculations were performed to produce rate estimates in nonbase counties, and incidence RRs were generated by dividing the rate in all base counties combined by the rate in all nonbase counties combined. Poison regression was used to calculate age-adjusted RR estimates for all ages combined.

In the second analysis, incidence RR estimates were calculated for individual counties. This was done by dividing the rate in each base county by the rate in all nonbase counties. Incidence RRs were calculated by individual calendar year and for all years combined using the Poisson model.

In the third analysis, we attempted to evaluate whether the location of a military base in an urban versus a rural area may affect leukemia risks. This was done by grouping counties on population density, defined as the total population of the county divided by the area of the county in square miles using data from the year 2000 U.S. Census. Rural counties were defined as those with a population density of less than 200 people per square mile.

Several bases included in this report had closed or realigned during the years covered by the SEER and CCR registries (DefenseLink 1998). In our initial set of analyses, counties with closed bases were treated as base counties for the years the base was open but were excluded as either base or nonbase counties for the years the bases were closed. Although adverse health effects due to base-related exposures may have occurred after a base had closed, we felt this method was the most conservative because the latency of any potential effects was unknown. In addition, substantial changes in population could occur soon after a base is closed. This may involve not only military families but also on-site civilian employees and others who may be economically linked to the military base. If large numbers of people move out of an area where a base has recently closed, this could potentially bias our results. Regardless, we evaluated the impact of excluding closed bases by performing separate analyses where counties with closed bases were treated as base counties, regardless of the date of closure. Most bases had closed within 4 years of the final year covered by the CCR and SEER registries.

Results

The age-standardized incidence RR of childhood leukemia for Churchill County for 1999–2001 was 12.0 [95% confidence interval (CI), 6.0–21.4; 11 cases observed, 0.92 cases expected] compared with age-specific rates from SEER counties. The *p*-value based on the Poisson probability model was 4.3×10^{-9}. The age-adjusted incidence RR using SEER rates for comparison for the time period after the State of Nevada began its investigation was 11.2 (95% CI, 3.6–26.3; 5 cases observed, 0.44 expected; Poisson $p = 0.0001$). One of the children in the Churchill County cluster was diagnosed with acute myeloid leukemia (AML), and 10 were diagnosed with ALL. In the analysis confined to ALL, the age-standardized incidence RR for Churchill County for 1999–2001 was 14.3 (95% CI, 6.9–26.3; 10 cases observed, 0.70 cases expected) using age-specific ALL rates from SEER counties for comparison. Table 1 presents a comparison of the Churchill County cluster with other well-known clusters of childhood leukemia.

Tables 2 and 3 show the facilities included and excluded from the analysis of military aviation bases. Twenty counties, incorporating 22 military aviation facilities, were included as base counties. Table 4 shows the incidence RR estimates for childhood leukemia for counties with military aviation bases compared with counties without bases for all years combined for each registry. No increases in childhood leukemia were identified in any of the four individual age groups, or for all ages combined, in either the SEER or CCR areas. RR estimates for each individual county with a

Table 1. Comparison of the Churchill County cluster with other selected childhood leukemia clusters.

Location	RR	No.	Age (years)	Time frame	No. of years	*p*-Value[a]
Churchill County, NV	12.0[b]	11	0–19	1999–2001	3	4.3×10^{-9}
Niles, IL[c]	4.3	8	0–14	1956–1960	5	4.3×10^{-4}
Dounreay, UK[d]	9.75	5	0–24	1979–1984	6	1.9×10^{-4}
Woburn, MA[e]	2.26	12	0–19	1969–1979	11	8.3×10^{-3}
Sellafield, UK[f]	11.07	6	0–14	1963–1990	28	2.2×10^{-5}

[a]*p*-Values based on the Poisson probability distribution model. [b]Age-standardized incidence RR using SEER registry data for years 1996–2000 as the referent group. [c]Heath and Hasterlik 1963. [d]Heasman et al. 1986. [e]Lagakos et al. 1986. [f]Draper et al. 1993.

military aviation base are shown in Table 5. An elevated RR was identified for Bernalillo County (RR = 1.22; 95% CI, 1.04–1.41) using all nonbase CCR counties for comparison. In the analysis confined to base counties with low population densities, an increase was identified for ages 10–14 years in the CCR base counties compared with CCR nonbase counties (RR = 1.36; 95% CI, 1.02–1.83; Table 6). All other RR estimates had 95% CIs that included 1.0.

Similar results were found in analyses confined to ALL. Incidence RRs for ALL were elevated for Bernalillo County (RR = 1.25; 95% CI, 1.04–1.50) and for ages 10–14 years for base counties in the CCR (RR = 1.39; 95% CI, 0.98–1.98) compared with CCR nonbase counties. In all other analyses of ALL, 95% CIs included the null.

As shown in Table 2, nine bases included in this analysis had closed or were realigned an average of 3.25 years before 1998, the last year of CCR data. Incorporating these years had little impact on the results. For example, the relative risk estimate for 1988–1998 for ages 0–19 years in the CCR base counties compared with CCR nonbase counties remained at 1.01 (95% CI, 0.94–1.10) when the years after base closure were included in base county rate calculations. None of the eligible bases in the SEER areas had closed during the years covered in this analysis.

In the analysis of yearly RRs for each individual base county compared with all nonbase counties, the large majority of RRs were near 1.0 (data not shown). Several base counties had yearly incidence ratios greater than 3.0, but all of these involved three or fewer cases and all occurred in counties that also had yearly RR estimates at ≤ 0.5 in other years. For example, in 1997, Curry County had a 4.8 higher incidence of childhood leukemia compared with nonbase counties. However, this was based on only three cases, and one year later, no cases were diagnosed in this county.

Table 2. U.S. military aviation facilities included in the analysis, based on SEER and CCR data.

Base	SEER/CCR	County, state	Density[a]	Open
Alameda NAS	Both	Alameda, CA	1,957	Closed 1997
Castle AFB	CCR	Merced, CA	109	Closed 1995
Edwards AFB	CCR	Kern, CA	81	Yes
El Centro NAF	CCR	Imperial, CA	34	Yes
George AFB	CCR	San Bernardino, CA	85	Closed 1992
Lemoore NAS	CCR	Kings, CA	93	Yes
March AFB	CCR	Riverside, CA	214	Realignment 1996
Mather AFB	CCR	Sacramento, CA	1,267	Closed 1993
McClellan AFB	CCR	Sacramento, CA	1,267	Closed 2001
Miramar NAS	CCR	San Diego, CA	670	Realignment 1997
Moffet Field NAS	CCR	Santa Clara, CA	1,303	Closed 1994
North Island NAS	CCR	San Diego, CA	670	Yes
Norton AFB	CCR	San Bernardino, CA	85	Closed 1994
Point Mugu NAS	CCR	Ventura, CA	408	Yes
Travis AFB	CCR	Solano, CA	475	Yes
Atlanta NAS	SEER	Cobb, GA	1,786	Yes
Cannon AFB	SEER	Curry, NM	32	Yes
Hill AFB	SEER	Davis, Weber, UT	494	Yes
Holloman AFB	SEER	Otero, NM	9	Yes
Kirtland AFB	SEER	Bernalillo, NM	477	Yes
McChord AFB	SEER	Pierce, WA	417	Yes
Whidbey Island NAS	SEER	Island, WA	343	Yes

Abbreviations: AFB, Air Force base; NAF, naval airfield. [a]Population density of the county (people per square mile) from the 2000 U.S. Census (U.S. Census Bureau 2003a).

Table 3. U.S. military aviation facilities in CCR and SEER areas excluded from the analysis.

Aviation facility	SEER/CCR	County, state	Exclusion
Camp Pendleton, USMC	CCR	San Diego, CA	Rotary wing
El Toro Marine Corp Air Station, USMC	CCR	Orange, CA	Rotary wing
Fresno Air Terminal AGS, USAF	CCR	Fresno, CA	ANG
Los Alamitos AFRC, USAF	CCR	Orange, CA	AAF, AFRC
Los Angeles AFB, USAF	CCR	Los Angeles, CA	Space/missile research
North Highlands AGS, USAF	CCR	Sacramento, CA	ANG
Onizuka AFB, USAF	CCR	Santa Clara, CA	Space/missile research
Ontario IAP AGS, USAF	CCR	San Bernardino, CA	ANG
Tustin Marine Corps Air Station, USMC	CCR	Orange, CA	Rotary wing
Van Nuys Airport AGS, USAF	CCR	Los Angeles, CA	ANG
Vandenburg AFB, USAF	CCR	Santa Barbara, CA	Space/missile research
Bradley IAP AGS, USAF	SEER	Hartford, CT	ANG
Des Moines IAP AGS, USAF	SEER	Polk, IA	ANG
Dobbins ARB, USAF	SEER	Cobb, GA	ARB
McCollum AGS, USAF	SEER	Cobb, GA	ANG
Orange AGS, USAF	SEER	New Haven, CT	ANG
Salt Lake City IAP AGS, USAF	SEER	Salt Lake, UT	ANG
Selfridge AFB, USAF	SEER	Macomb, MI	ANG
Sioux City MAP AGS, USAF	SEER	Woodbury, IA	ANG

Abbreviations: AAF, Army airfield; AFB, Air Force base; AFRC, Armed Forces Reserve Center; AGS, Air Guard station; ANG, Air National Guard; ARB, Air Force Reserve base; IAP, international airport; MAP, municipal airport; USAF, U.S. Air Force; USMC, U.S. Marine Corp.

Discussion

The recent cluster of childhood leukemia cases in Churchill County represents a 12-fold increase above leukemia rates in SEER registries. The probability that this cluster would occur by chance is 4.3×10^{-9}, or about 1 in 232 million. Given that the U.S. population 0 to 19 years of age is 10,662 times larger than that of Churchill County (U.S. Census Bureau 2003a), we would expect a cluster of this size to occur in the United States by chance alone about once every 22,000 years. In contrast, the *p*-value for the cluster in Woburn, Massachusetts, the basis of the novel *A Civil Action* (Harr 1995), was 0.0084 (Table 1), or about 1 in 120 (Lagakos et al. 1986).

Importantly, the rate of childhood leukemia seen in Churchill County remained markedly elevated after the State of Nevada began its investigation. Thus, the elevated rates identified in this report are not based solely on *post hoc* hypothesis testing. Given these findings, it appears very unlikely that the Churchill County cluster was attributed only to chance.

No new cases have been diagnosed among Churchill County residents since 2001, although one former resident was diagnosed with leukemia in 2002. Thus, it appears that the cluster among Churchill County residents has spanned a period of 3 years. Table 1 shows a comparison of the Churchill County cluster with other well-known childhood leukemia clusters. By virtue of its large magnitude and short time span, the Churchill County cases seem to represent one of the most unique clusters of childhood cancer ever reported.

One of the goals of this investigation was to evaluate whether the large increases in childhood leukemia risks near NAS Fallon might have occurred near other military aviation facilities. In this analysis, no clear association was found between residence in a county containing a military aviation base and risk of childhood leukemia. Elevated RRs were identified in a few subgroup analyses. However, given the large number of analyses performed and the lack of consistent findings across subgroups, these elevations could be due to chance.

One strength of this investigation was the use of cancer registry data from SEER and CCR. Both registries provide a readily accessible source of incident cancer data for a wide geographic area and for a relatively broad number of years. Because of the lack of a nationwide cancer registry and current unavailability of county-specific data after 1999, we were unable to assess all military aviation facilities and unable to assess more recent effects. Despite this, the use of SEER and CCR data provided a relatively quick and simple, albeit limited, method of evaluating whether the elevated rates of childhood leukemia in Churchill County might be more widespread.

A cause of the Churchill County cases has not been identified. The CDC has recently completed the first portion of a large cross-sectional investigation of the cluster area (CDC 2003). Biologic samples collected from cases and controls, and the families of both groups, were analyzed for 16 metals, 31 nonpersistent pesticides and metabolites, 11 persistent pesticides, 36 polychorinated biphenyls (PCBs), 12 volatile organic compounds, and six viruses. Elevated levels of tungsten, arsenic, two chlorophenol pesticides, and 1,1-dichloro-2,2-bis(*p*-chlorophenyl)-ethylene (DDE) were found community-wide, but none were elevated in cases compared with controls. No association was found with Epstein-Barr Virus, human T-lymphotropic virus type-1, or other retroviruses. Levels of naturally occurring arsenic in the public water supplies of Fallon are about twice the current U.S. standard (Focazio et al. 2000). However, these levels have been relatively unchanged over many decades and no clear link has been established between ingested arsenic and elevated rates of leukemia [Focazio et al. 2000; Moore et al. 2002; National Research Council (NRC) 1999].

Population mixing has been hypothesized as a possible cause of the Churchill County cluster. In several studies, increased rates of childhood leukemia were found in areas experiencing large-scale population influxes. These areas include rural new towns, towns with large increases in commuting, areas with large numbers of military personnel or wartime evacuees, and areas with large numbers of migrant construction workers (Alexander et al. 1997; Kinlen 1995; Kinlen and Petridou 1995; Li et al. 1998; Stiller and Boyle 1996). For example, in a study of 14 British rural towns newly developed in the period 1946–1950, Kinlen et al. (1990) reported relative risks of childhood leukemia of 2.75 ($p < 0.01$) for ages 0–4 years and 1.58 ($p < 0.05$) for ages 0–14 years. The large numbers of military personnel who come in and out of NAS Fallon each year would seem to provide ample opportunity for the introduction of new infectious agents. Approximately 55,000 personnel attend training operations at NAS Fallon annually, each staying an average of 14 days. In most studies of population mixing, the large influxes occurred just before periods when leukemia

Table 4. Age-adjusted RRs of childhood leukemia in counties with military aviation bases, based on SEER and CCR data.

	Counties with air bases		Counties without air bases		
Age (years)	No.	Person-years	No.	Person-years	RR[a] (95% CI)
SEER					
0–4	451	6,386,081	2,136	32,053,769	1.06 (0.96–1.17)
5–9	225	6,095,212	1,122	31,923,232	1.05 (0.91–1.21)
10–14	140	6,067,279	787	33,041,840	0.97 (0.81–1.16)
15–19	139	6,282,183	787	34,168,595	0.96 (0.80–1.15)
All (0–19)	955	24,830,756	4,832	131,187,436	1.04 (0.97–1.12)
CCR					
0–4	705	9,667,251	446	5,575,697	0.91 (0.81–1.03)
5–9	395	8,713,971	214	5,400,364	1.14 (0.97–1.35)
10–14	228	7,738,112	134	5,009,599	1.10 (0.89–1.36)
15–19	216	7,473,471	152	4,822,352	0.92 (0.75–1.13)
All (0–19)	1,544	33,592,804	946	20,808,012	1.01 (0.93–1.10)
Churchill County					
All (0–19)[b]	11	22,644			12.0 (6.0–21.4)

[a]Age-standardized incidence RR for counties with military aviation bases using rates in all SEER (1973–1999) and CCR (1992–1998) counties without bases as the respective referent group. [b]Age-standardized incidence RR for Churchill County, 1999–2001, using SEER registry data for years 1996–2000 as the referent group.

Table 5. Age-adjusted RRs of childhood leukemia in individual counties with military aviation bases, based on SEER and CCR data.

County	No.	Person-years	RR[a] (95% CI)
SEER			
Alameda, CA	310	8,409,581	1.00 (0.89–1.12)
Bernalillo, NM	172	3,843,281	1.22 (1.04–1.41)
Cobb, GA	105	2,952,786	0.97 (0.80–1.17)
Curry, NM	10	424,363	0.64 (0.34–1.19)
Davis and Weber, UT	136	3,615,670	1.02 (0.86–1.21)
Island, WA	13	408,770	0.86 (0.50–1.49)
Otero, NM	14	475,246	0.80 (0.47–1.35)
Pierce, WA	173	4,508,106	1.04 (0.90–1.21)
CCR			
Alameda, CA	191	4,030,004	1.04 (0.89–1.22)
Imperial, CA	29	515,879	1.24 (0.85–1.79)
Kern, CA	105	2,250,151	1.03 (0.84–1.26)
Kings, CA	41	951,207	0.95 (0.69–1.30)
Merced, CA	45	787,174	1.26 (0.93–1.70)
Riverside, CA	195	4,537,685	0.95 (0.81–1.10)
Sacramento, CA	154	3,603,639	0.94 (0.79–1.11)
San Bernardino, CA	277	5,883,799	1.04 (0.91–1.18)
San Diego, CA	377	8,354,212	0.99 (0.88–1.12)
Santa Clara, CA	227	4,784,558	1.04 (0.90–1.21)
Solano, CA	61	1,261,367	1.06 (0.82–1.38)
Ventura, CA	110	2,347,259	1.03 (0.85–1.26)
Churchill County[b]	11	22,644	12.0 (6.0–21.4)

[a]Age-standardized incidence RR for individual counties with military aviation bases using rates in all SEER (1973–1999) and CCR (1992–1998) counties without bases as the respective referent group. [b]Age-standardized incidence RR for Churchill County, 1999–2001, using SEER registry data for years 1996–2000 as the referent group.

Table 6. Age-adjusted RRs of childhood leukemia in counties with military aviation bases and low population density, based on SEER and CCR data.

	Counties with air bases		Counties without air bases		
Age (years)	No.	Person-years	No.	Person-years	RR[a] (95% CI)
SEER					
0–4	8	237,653	2,136	32,053,769	0.51 (0.25–1.01)
5–9	4	222,714	1,122	31,923,232	0.51 (0.19–1.36)
10–14	5	218,046	787	33,041,840	0.96 (0.40–2.32)
15–19	7	221,208	787	34,168,595	1.37 (0.65–2.89)
All (0–19)	24	899,621	4,832	131,187,436	0.72 (0.48–1.08)
CCR					
0–4	157	2,249,046	446	5,575,697	0.87 (0.73–1.05)
5–9	97	2,052,710	214	5,400,364	1.19 (0.94–1.52)
10–14	68	1,862,587	134	5,009,599	1.36 (1.02–1.83)
15–19	48	1,688,677	152	4,822,352	0.90 (0.65–1.25)
All (0–19)	370	7,853,019	946	20,808,012	1.04 (0.92–1.17)

[a]Age-standardized incidence RR for counties with military aviation bases and low population density using rates in all SEER (1973–1999) and CCR (1992–1998) counties without bases as the respective referent group.

risks were elevated (Kinlen 1995). At NAS Fallon, large movements of personnel have occurred for at least the past 10 years (U.S. Navy 2002a). The arrival of the Navy Fighter Weapons School (nicknamed "Topgun") and the Carrier Airborne Early Warning Weapons School at NAS Fallon in 1996 resulted in only moderate increases in the numbers of personnel.

In most studies of population mixing, relative risks have been near 2.0. In both *post hoc* and *a priori* analyses, the relative risk we identified for the Churchill County cluster is substantially higher than this. As discussed by several authors, one may find higher relative risks depending on the boundaries of time and space used to analyze a cluster. This can be especially true in *post hoc* analyses of known clusters because the specific region and time frame being assessed is typically defined by the cluster (Doll 1999; Neutra 1990; Neutra et al. 1992; Rothman 1990; Waller 2000). For example, in an analysis of all parishes within a 10-km radius of a power station in Drax, North Yorkshire, United Kingdom, Kinlen et al. (1995) reported a relative risk of 1.5 based on 22 observed cases. However, in a *post hoc* analysis that focused on one particular parish with five cases, a relative risk of 7.9 was reported.

Another hypothesis that was proposed as a cause of the Churchill County cluster was exposure to JP-8 jet fuel, or benzene, a minor component of JP-8 (Carlton and Smith 2000; U.S. Navy 2002b). Several studies have shown that JP-8 can affect immune system cells and may be genotoxic, although no clear link has been established with leukemia in humans or animals (Grant et al. 2001; Harris et al. 1997a, 1997b, 2000, 2001; Jackman et al. 2002; Rhodes et al. 2003; Ullrich 1999). Benzene has been associated with AML and possibly ALL in occupationally exposed cohorts (Hayes et al. 2001; Savitz and Andrews 1997). One of the Churchill County leukemia cases is AML; however, the remaining 10 are ALL, and the five cases among former residents are all cases of ALL (NSHD 2003). Environmental exposures to benzene are typically well below those associated with leukemia risks in occupational settings (Duarte-Davidson et al. 2001), and to date, no evidence of significant benzene or JP-8 exposure has been linked to the Churchill County cases (CDC 2003). In addition, the high relative risks we have identified for Churchill County, combined with the lack of increased risks in other base counties with similar military related exposures, provides further evidence that a routine exposure specifically related to military aviation was not the cause of the Churchill County cluster.

In this analysis, we found no evidence that large widespread increases in the risks of childhood leukemia have occurred in U.S. counties with military aviation facilities. However, this investigation was limited in its ability to identify small isolated increases. One potential limiting factor was that the unit of exposure was restricted to the county level. If significant exposures were occurring near bases, it could be that only those children living in close proximity to the base, or those with a parent actually working on the base, were truly exposed. If so, any increase in leukemia associated with the base might be diluted by the cancer experience of the rest of the county. None of the counties with bases included in this analysis had a population or population density as low as that of Churchill County. However, many of the base counties we assessed were small enough that, on average, fewer than three cases of leukemia were diagnosed each year. In these counties, a substantial increase in cases, such as the eight new cases diagnosed in Churchill County in the year 2000, could have been detected by the methods used here. Three of the base counties we analyzed had individual yearly RR estimates above 3.0. However, all of these were based on few cases, and all occurred in counties that also had some yearly relative risk estimates ≤ 0.5 in other years. None of the base counties had RR estimates that approached those seen in Churchill County.

In this analysis, exposure was based on county of residence at the time of diagnosis. Migration of families in and out of the study area may have also limited our ability to detect effects, although in the United States, the rate of migration of families with children is low. According to data from the U.S. Census, only 6% of children 1–19 years of age move across counties each year (U.S. Census Bureau 2003b). Military families likely move more often. However, in Churchill County, only three of the 16 total cases were from military families (NSHD 2003).

We could not obtain detailed data on specific base activities or specific chemical exposures. Many of the exposures that occur near military aviation bases may occur at other facilities such as municipal airports, heavily industrialized areas, or nonaviation military bases. Including counties with these facilities among our nonbase counties may have biased RR estimates toward the null. We also did not have access to specific data on yearly troop movements at each military base. Although most military aviation bases have influxes of personnel from diverse locations, few appear to have the consistently high troop movements seen at NAS Fallon (GlobalSecurity.org 2003). Including bases with low rates of migration would have biased any effects related to population mixing towards the null and thus limited our ability to evaluate this hypothesis.

In summary, the cluster of childhood leukemia cases in Churchill County appears to be one of the most unusual childhood cancer clusters ever reported and may warrant further investigation. Our study of risks near other military aviation bases was limited to an evaluation of exposure based on county of residence, so specific exposures such as jet fuel and population mixing could not be precisely evaluated. However, we found no evidence of consistent associations between the risk of childhood leukemia and residence near other military aviation facilities and no evidence that the childhood cancer experience near NAS Fallon was much more widespread. Given the results of previous studies of population mixing, the large troop movements at many military facilities, and the far-ranging and diverse locations traveled by military aviators and other personnel, a more comprehensive study of population mixing in areas near military facilities may be warranted. In addition, several studies have shown that certain specific genetic changes play an important role in the development of leukemia (Greaves 1999). Given the unusual clustering of the Churchill County cases, further in-depth analyses of tumor and nontumor genetics might provide evidence of a common link between these cases and insight into the cause of this cluster and the causes of childhood leukemia in general.

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